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Points:

- Medical R&D SBIR Programs (NIH, DOD) were designed to initiate R&D on products for diseases of importance to the U.S. public health. Program requires companies to (a) show evidence of follow-on funding for product commercialization and (b) commercialize a product from at least one Phase II grant (or no more SBIR grants can be awarded).
- Sources of follow-on funding are limited in the high-risk clinical phase of product development because of the cost of these development tasks (hundreds of millions of dollars): VC are virtually only source of capital in this quantity.
- SBIR and VC moneys do not co-mingle: they are used sequentially for research (SBIR) and clinical trials/commercialization (VC): both are essential to bring products to marketplace for use by physicians/patients.
- SBIR grants should focus on the best science, regardless of VC financing of companies.

Mr. Chairman and Committee:
Thank you for offering me the opportunity to provide information about the impact of the ruling on eligibility of VC-backed companies for SBIR grants on my company and my industry.

Sequella, Inc. is an 8 year-old biopharmaceutical company discovering and developing products for the diagnosis and control of tuberculosis (TB), a global health threat of truly awesome proportions: 2 billion people (one of every three in the world) are infected with the bacterium today, and 15% of these people (or 300 million) will come down with fulminant and lethal TB in their lifetime, the next 30-50 years. There are now nearly 10 million new cases of TB every year and over 2 million deaths annually. TB is an aerosol-transmitted debilitating disease that is listed as a biothreat agent of concern to the U.S. government.

Although we have indigenous TB almost under control in our country, we exist in a global economy and we import TB on a daily basis inside people who travel for business or pleasure or immigrate for permanent citizenship from areas of the world that are overwhelmed by this disease. Until we solve the global problem of TB, our country is at risk for the importation of drug-resistant TB from elsewhere that will quickly undermine our public health efforts at control. Just one example: New York City closed down their $50 million/year TB control program in the late 1980s. Within three years of closure, New York City underwent a mini-epidemic of TB and drug-resistant TB that cost the city over $1 billion dollars and two years to control. TB is not a disease to ignore or underestimate.

Sequella was established as a for-profit company in 1997 to solve a problem that the U.S. Public Health Service (CDC and NIH) recognized as a time-bomb: the re-asserting of control for resurgent TB in the 1990s in New York City and other urban centers in the U.S. was strongly hampered by the techniques available to diagnose and treat the disease, techniques which are 50-100 years old. Although TB was the #1 killer of U.S. citizens prior to 1950, the antibiotic era of 1950-1990 allowed us to become complaisant about infectious diseases, and no new antibiotics were discovered or developed for TB since mid-1970s. Sequella was established to reverse this industry trend.

Sequella has been financed over the last 8 years through Founder and Director equity investments, investment by Angel investors, and a variety of competitive scientific research grants, including grants and contracts from the SBIR program at the National Institutes of Health (NIH). We have competed for and received SBIR funding for diagnostics, devices, vaccines and drugs, all focused on TB: the total amount of funding under the SBIR grant/contract program alone was about $6.5 million (see Table 1), out of a total of $18 million raised overall for the company.

Table1. *List of SBIR grant awards to Sequella, Inc*.

Grant	Type	Title	Submitted	Awarded	Per Year	Duration	TOTAL ($)
R43A143812	SBIR	Antibody-based Diagnostic for TB in non-human primates	12/15/97	9/1/98	$100,000	6 months	$100,000
R43AI/GM46094	SBIR	Shikimate Enzymes as Novel Tuberculosis Drug Targets	12/15/98	7/1/99	$100,000	1 year	$100,000
R43AI46062	SBIR	Electronic Monitoring of Compliance with TB Chemotherapy	12/15/98	9/31/00	$300,000	1 year	$300,000
R43AI48973	SBIR	Commercial Development of the Bronx Box	8/1/00	2/15/01	$300,000	1 year	$300,000
R43AI49608	SBIR	A new Tuberculin for the Diagnosis of TB	8/1/00	9/15 01	$300,000	1 year	$300,000
R43AI50271	SBIR	A rapid lateral-flow Test for TB in Nonhuman Primates	12/1/00	9/15/01	$168,000	1 year	$168,000
R43AI50273	SBIR	Transdermal Test for Active TB	12/1/01	9/15/02	$300,000	1 year	$300.000
N43AA23006	SBIR	Transderm noninvasive monitor	3/1/02	9/14/03	$100,000	1 year	$100,000
R44AI48973	SBIR	Commercial Development of Bronx Box Phase II	9/30/02	12/31/04	$600,000/yr	2+ year	$1,300,000
R43AI051832	SBIR	BCG + Hsp TB Vaccine	3/15/03	5/15/04	$300,000	1 year	$300,000
N44AA33009	SBIR	Transdermal noninvasive monitor Phase II	9/25/03	9/24/05	$469,575/yr	2 years	$939,150
R44AI50271	SBIR	A rapid lateral-flow Test for TB in Nonhuman Primates Phase II	9/25/03	9/24/05	$986,375/yr	2 years	$1,972,751
R43AI060250	SBIR	Dipiperidine Drug Class	9/1/04	9/1/05	$300,000	1 year	$300,000

Despite the healthy success of SBIR grant competition, Sequella will require over $10 million in additional funds in the next two years to complete the clinical trials of its new and more effective diagnostic and initiate the clinical trials of its new drug that, in animals, is both more effective than existing drugs and shortens the treatment time for cure.

The SBIR programs at NIH are designed to stimulate research and development of products for diseases of interest to the federal government, regardless of commercial interests in such products. TB is such a disease: a U.S. problem with little ongoing commercial effort. The amount of money and structure of SBIR grants ($75K-$300K Phase I; $750K-$2M Phase II) is sufficient only to start the process of drug, diagnostic, or vaccine discovery and development. The overall costs of development of a new product from the time that the research looks promising is overwhelmingly large, and the money to cover these costs is extremely difficult to find:

- Preclinical toxicity studies for drugs/vaccines range from $2M-$5M in cost/product candidate
- Clinical trials for a single drug/vaccine range from $30M to $150M/product, depending upon indication

Non-SBIR money is clearly required to bridge the funding gap to get a product to the patients it is to serve: the only source for that large an amount of money going to a high-risk venture such as drug development (with 1 in 5000 success rate) is venture capital (VC). VC money is for clinical development and commercialization, not the high-risk discovery research or early translational research before the clinic: research into new targets of interest to government is last on priority list with VC money, and rightly so. They must push companies to develop a product revenue stream so that they can exit their high-risk investment with an acceptable return on investment.

Specific impact of the eligibility ruling: Sequella, Inc. has two SBIR grant applications (a Phase I for $300K and a Phase II for $1.6M) that are in a queue for funding in this FY2005. Funding is expected by late summer. Sequella is also completing its first VC financing to fund the clinical trials of the new TB drug and the new TB diagnostic that were developed with NIH SBIR and other grant funds. The loss to Sequella of the ~$2M SBIR grants for its portfolio products NOT ready for clinical trials will be a significant loss to the company and will not be replaced by VC financing. Without SBIR support, we would not have spent the time and energy on TB, a disease that is not considered a commercial opportunity in the U.S. Without the grant support in the future, our remarkable research success in finding new diagnostics, drugs, and vaccines for important non-commercial diseases of importance to the U.S. will stop.

In Sequella, and I suspect in most other small biotechnology companies, the SBIR and VC money will not co-mingle, but will be used sequentially for product development: research (SBIR) funding will drive new product identification; commercialization (VC) funding will bring the identified product to market for use by patients. Both sources of capital are critical for product success. Most VC-backed biotechnology companies remain small businesses (many of them very small: Sequella has only 17 employees), and the addition of VC to the Board or VC commercialization funds to the treasury does not make them any larger or less in need of discovery research funding.

I have heard comments that the SBIR set-aside moneys are only 2.5% of grant support available at the NIH. I continue to review grants for the NIH in non-SBIR programs, and I can tell you from personal experience that companies do not compete well in this arena. The reason? We do not do hypothesis-driven research. Our research is governed by rules and regulations of the FDA for product development, and even the discovery research we do does not address fundamental biology, but product-oriented processes not amenable to review by academicians who drive the R01 granting processes at the NIH.

Competition with other small business industries does not exist for NIH SBIR programs: only biotechnology/biopharma companies compete for the dedicated small business set-aside moneys from NIH and DOD for medical research. Thus, the argument that VC-backed small biotechnology companies in medical research are unfairly competing for small business funds in general is erroneous: only science-based companies can compete for the NIH/DOD medical research funds. Although having VC investment provides an opportunity to be a successful company that commercializes products, VC investment does *not* provide a scientific advantage for companies: science is reviewed for its merits, not its financial backing. Good science that is competitive can come from VC-backed companies or companies that are not VC-backed. Sequella is an example of the latter: we have been highly successful at grant competitions, although we are not yet VC financed. I am absolutely sure that we will be as competitive when we have VC funding. Competition is based on scientific merit, and for the best science to prevail, we should all (VC-backed or not) be in the mix.

The country will only benefit if all the best product-oriented science is funded, but it will also only benefit if that science is transformed from a promise to a product, and that will happen most efficiently in VC-backed companies with sufficient funds to make it though the costly clinical development process.

Thank you again for the opportunity to express my views before the Committee.